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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/031,145

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Nicole Zitzmann

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FOLEY AND LARDNER LLP

SUITE 500

3000 K STREET NW

WASHINGTON, DC 20007

EXAMINER

WILLIAMS, LEONARD M

ART UNIT

PAPER NUMBER

1617

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DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/031,145	<b>Applicant(s)</b> ZITZMANN ET AL.	
	<b>Examiner</b> Leonard M. Williams	<b>Art Unit</b> 1617.	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS; WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 32, 33 and 35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 32-33 and 35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

Detailed Action

***Response to Amendments/Arguments***

No amendments have been made to the claims. Claims 32-33 and 35 are pending.

Applicant's arguments filed 08/31/2007 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The applicant's have argued, on page 6, that Van den Broek teaches away from performing the modifications suggested by stating "modification of the hydroxyl function(s) is detrimental to the activity of the compound". The applicant's have not pointed where in the reference this statement is made and the examiner can not find any indication of such a statement in the reference. As indicated in the rejection, Van den Broek teaches that toxicity is associated with the amphiphilicity of the compound and that by changing the amphiphilicity the toxicity can be adjusted. Thus the reference is provided to demonstrate this property and not for the activity of the compounds in the assays per se.

For the reasons detailed above and for the reasons of record the rejections of the last rejection are maintained and reproduced below. This action is made **final**.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32-33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacob et al. (WO99/24401), in view of Platt et al. (US Patent NO. 6462197) and Defoin et al. (6-Deoxy-Nojirimycin and 6-Deoxy-gulo-Nojirimycin in the racemic and D-series, D-Fuco-Nojirimycin and their 1-Deoxyderivatives via Hetero-Diels-Alder Cycloadditions, 1997, Tetrahedron, vol. 53, No. 40, pp. 13783-13796) and further in view of van den Broek et al. (Synthesis of oxygen-substituted N-alkyl 1-deoxynojirimycin derivatives: aza sugar  $\alpha$ -glucosidase inhibitors showing antiviral (HIV-1) and immunosuppressive activity, Recl. Trav. Chim. Pays-bas, 1994, vol. 113, pp. 507-5166).

Jacob et al. teach, on pages 14-15, N-substituted-1,5-dideoxy-1,5-imino-D-glucose and galactose compounds of formula I wherein R is selected from C1-C20 alkyl groups containing 1-5 oxygen atoms (oxa derivatives) with preferred R oxa derivatives being 3-oxanonyl, 3-oxadecyl, 7-oxanonyl and 7-oxadecyl.

Jacob et al. does not teach N-nonyl-1,5,6-trideoxy-1,5-imino-D-galactitol nor N-(7-oxa-nonyl)-1,5,6-trideoxy-1,5-imino-D-galactitol compounds.

Platt et al. teach, in col. 1 lines 10-65, novel N-alkyl derivatives of deoxygalactonojirimycin (DGJ) in which the alkyl group is from 3-6 atoms. The inhibitory activity of these compounds have lead to their development as antihyperglycemic agents and anti-viral agents. DGJ has been shown to have better inhibitory activity compared to N-alkyl-deoxynojirimycin (DNJ).

DeFoin et al. teach, on pages 13783-13785, that aminosugars are rather unstable compounds and can be converted into their 1-deoxy derivatives which possess similar inhibitory activity properties. 1-deoxy-L-fuco-nojirimycin is described as a potent  $\alpha$ -fucosidase inhibitor. L-fucose is equal to 6-deoxy-L-galactose thus 1-deoxy-L-fuco-nojirimycin is equivalent to 1,6-dideoxy-L-galacto-nojirimycin (or 1,5,6-trideoxy-L-galactonojirimycin). It is taught that 1,6-dideoxy-nojirimycin is known to possess inhibitory activity similar (though less effective) to 1-deoxy-nojirimycin. It is further taught that D-fuco-nojirimycin (equals 6-deoxy-D-galacto-nojirimycin) and 1,6-dideoxy-D-fuco-nojirimycin (equals 1,6-dideoxy-D-galacto-nojirimycin) can be readily synthesized.

van den Broek et al. teach, on page 508, that N-decyl-deoxynojirimycin is a potent  $\alpha$ -glucosidase inhibitor in the HepG2 assay but showed significant toxicity. The toxicity was believed to be associated with the amphiphilicity of the molecule. In order to reduce the amphiphilicity of the compound either the N-decyl side chain's lipophilicity can be decreased or the aza-sugar ring can have its lipophilicity increased. The changing of the N-decyl group with N-(7-oxadecyl) was performed to reduce the side chain's lipophilicity. It would also be possible to remove one or more of the hydroxyl groups on the aza-sugar in order to achieve an increased lipophilicity of the aza-sugar.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the 1,5-dideoxy and 1,5,6-trideoxy alditols with the D-galacto configuration of Platt et al. and DeFoin et al. in the Jacob et al. formula 1 compounds as the Jacob et al. compounds differ only in that they disclose only 1,5-dideoxy alditols.

One would have been motivated to make such a change as van den Broek et al. demonstrate that changes in the aza-sugar portion of deoxynorjirimycin that would increase its lipophilicity would alter the toxicity profiles of the compounds. Removal of a hydroxyl group at the 6 position would result in an increase in the lipophilicity of the aza-sugar. Further Platt et al. demonstrated that the deoxygalactonojirimycin compounds demonstrated increased inhibition compared to deoxynojirimycin. One would expect a reasonable chance of success as DeFoin et al. details the synthesis of the 1,5,6-trideoxy D-galactitol compounds and Jacob et al. and Platt et al. demonstrate the introduction of alkyl moieties on the ring nitrogen. Further Jacob et al. details the synthesis of 1,5-dideoxy D-galactitol compounds the process of which could easily be modified to utilize DeFoin et al. 1,5,6-trideoxy D-galactitol (equals 1,6-dideoxy-D-fuco) moieties.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of


the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LMW

  
SREENI PADMANABHAN  
SUPERVISORY PATENT EXAMINER